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EXAMINER

LI, BAO Q

ART UNIT PAPER NUMBER

1648

DATE MAILED: 08/27/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/074,620

Applicant(s)

GREEN ET AL.

Examiner

Bao Qun Li

Art Unit

1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 01 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 6-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Claims 1-39 are pending.

#### ***Election/Restrictions***

1. Applicant's election with traverse of Group I, claims 1-5 in Paper No. 11 is acknowledged. The traversal is on the ground(s) that all groups are classified in the same class and searching all groups will not place a serious burden on the examiner even if the claims are to represent independent or distinct inventions in the current application.
2. Applicants' argument has been fully considered; however, it is not found persuasive because classification is not only one criterion for the election/Restriction. There are multiple patentability issues that should be considered during the Election/Restrictions requirement. Since the claimed invention are directed several compositions and methods comprising use of different probe or pair of primers independently, each of them has different structure and patentable weight, which require different sequence search and therefore, it constitute a serious burden for the Office to search all structurally non-related sequences together. Hence, only elected claims 1-5 are considered.
3. Applicants failed to response to the previous Office Action for further electing one pair of primer sequences. However, they argue that this election is not proper because the selection of primers and probes are member of a Markush group. A reconsideration of a species election of a pair of primers or probe is required.
4. Applicants' argument has been respectfully considered. The Applicants representative attorney, Stephen R Albainy-Jenei has been contacted. During a telephone conversation with Stephen R Albainy-Jenei on August 19 2003, a provisional election was made on species of SEQ ID NOs: 1 and 2 with traverse to prosecute the invention of group I, claims 1-5. Affirmation of this election must be made by applicants in replying to this Office action. SEQ ID Nos 5 and 6 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.
5. Claims 1-5 in the scope of SEQ ID Nos 1 and 2 are considered before the examiner. The SEQ ID NO: 5 & 6 and their mutants in claims 3-5 are withdrawn from the consideration.

Art Unit: 1648

6. Applicants are reminded to amend the claims 1-5 to the scope of SEQ ID Nos 1 & 2 for reflecting the examination on the merits and cancel the claims 6-39 drawn to the non-elected groups.

***Specification***

7. The disclosure is objected to because of the following informalities: in Table III, the length of primer of SEQ ID NO: 1 is incorrectly written as 20. However, it should be written as 18. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1 and 3-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a probe or a pair of primers consisting of SEQ ID NO: 1 & 2, which are able to specifically hybridize and detect Epstein-Barr virus (EBV) under a stringent hybridization condition, does not reasonably provide enablement for having any or all nucleic acid sequence using a probe having as low as 80% homology or any or all pair of primers comprising or consisting essential of a pair of nucleotide sequences, wherein the pair of nucleotide sequences have as low as 95% homology to SEQ ID NO: 1 and 2 or a base nucleic acid change of SEQ ID NO: 1 and 2, which is able to specifically detect EBV virus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

10. Applicants are reminded that because the claims 3-5 use an open language "comprising" or consisting essential of <sup>off</sup> to describe the claimed nucleotide structures and do not define what the percentage of complementary or hybridization condition in the claims, Office interprets claims 3-5 as any purified or isolated pair of primers in any length as long as each of them

Art Unit: 1648

comprises a nucleotide sequence having 95% to the sequences of SQ ID NO: 1 and 2 or having one base of nucleotide change.

11. Please see MPEP regarding to the recitation of “comprising” or consisting essential of” in the claims:

12. 2111.03 Transitional Phrases

13. The transitional phrases “comprising”, “consisting essentially of” and “consisting of” define the scope of a claim with respect to what unrecited additional components or steps, if any, are excluded from the scope of the claim.

14. The transitional term “comprising”, which is synonymous with “including,” “containing,” or “characterized by,” is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., *Genentech, Inc. v. Chiron Corp.*, 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) (“Comprising” is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.); *Molculon Research Corp. v. CBS, Inc.*, 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); *In re Baxter*, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) (“comprising” leaves “the claim open for the inclusion of unspecified ingredients even in major amounts”).

15. The transitional phrase “consisting of” excludes any element, step, or ingredient not specified in the claim. *In re Gray*, 53 F.2d 520, 11 USPQ 255 (CCPA 1931); *Ex parte Davis*, 80 USPQ 448, 450 (Bd. App. 1948) (“consisting of” defined as “closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith.”). A claim which depends from a claim which “consists of” the recited elements or steps cannot add an element or step. When the phrase “consists of” appears in a clause of the body of a claim, rather than immediately following the preamble, it limits only the element set forth in that clause; other elements are not excluded from the claim as a whole. *Mannesmann Demag Corp. v. Engineered Metal Products Co.*, 793 F.2d 1279, 230 USPQ 45 (Fed. Cir. 1986).

16. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See *United States v. Theketronic Inc.*, 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

17. 1) & 2). State of art and Unpredictability.

Art Unit: 1648

18. Regarding to the specifically detection of EBA by a using a probe hybridization, the state of art teaches that a probe is a DNA sequence used in a hybridization assay and the result of the hybridization is influenced by these important temperature and conditions significantly. The selections of these important temperature and conditions depend on the length of the target sequence, the size of the probe, the content of nucleotides. For example, hybridization of 14 bases of nucleotides can be done in the room temperature, whereas hybridization of 23 bases of nucleotides needs to be kept at 48°C. The melting temperature ( $T_m$ ) between the two complementary nucleic acid sequences also varies with the length of nucleic acid sequence, e.g. for a 20 nucleotides, the  $T_m$  is about 40°C, whereas the  $T_m$  for a more than 30 base of polynucleotide is above 70 °C as evidenced by Ausubel et al. (Short Protocols in Molecular Biology, 1999, 4th Edition, Edited by Ausubel et al. Published by John Wiley & Sons, Inc., page 6-6 to 6-8). In addition, the important temperature of  $T_m$  is dependent upon the oligonucleotide sequence and the composition of the solvent as taught by Wetmur (Critical Reviews in Biochemistry and Molecular Biology 1991, vol. 26, pp. 227-259). He teaches that the polynucleotide duplex may be DNA, RNA or RNA-DNA hybrid and may vary in base composition, expressed as % G+C. Nevertheless, the  $T_m$  varies according to the percentage of G+C in the content of the sequence (See page 228).

19. Therefore, it is unpredictable that any nucleotide sequence comprising 80% of homology to SEQ ID NO: 1 or 2 will be able to specifically hybridize EBV because the size of probe and content of nucleotide sequence determine a different condition for a specific hybridization.

20. Regarding to the primer, the state of art teaches that the ability of an oligonucleotide to act as a primer in DNA synthesis also depends on several factors: kinetics of association and dissociation of the primer: template duplex under the annealing and extension conditions, the effects of mismatched bases and their locations on the duplex stability, and the efficient with which the polymerase can recognize and extend from a mismatched duplex. In general, single base pair mismatched at or near the terminal 3' base of primer is know to affect the ability of the polymerase to bind and extend from the primer: template and therefore should have a significant effect on the efficiency of the primer reaction (Please see Sorge et al. WO 95/16028A1, see lines 7-22 on page 10). For example, Sorge et al. disclosed that no product or a lot of failure products

Art Unit: 1648

were produced due to either 3' primer: template mismatches (See example, 4 on pages 24-25 and Table 10 on page 25, especially lines 19-24 on page 24) or none-3' primer: template mismatches (See example 5 and Table 11 on page 26-27, especially, line 118-20 on page 27).

21. Because Office interprets that the claimed nucleotide sequence can be any size longer than SEQ ID NO: 1 or 2 due to the open language of the claims, it may have more mismatches beyond that 95% nucleotide sequence fragment in turn of the whole primer sequence. Therefore, it is very unpredictable for using any or all claimed nucleotide sequence to specifically detect the EBV by PCR.

22. 3) & 4) Number of working examples and amount of guidance.

23. Specification only teaches that a pair of nucleotide sequence consisting of SEQ ID NOs: 1 and 2 are able to be used as a pair of primers for detecting EBV under a condition as listed in Table IV & V (Pages 44-45).

24. However, specification does not teach that any other sequence is able to specifically detect EBV.

25. Furthermore, Applicants are reminded that the identity, homology or sequence similarity can be calculated by a variety of different methods, whereby the calculated identity between two sequences will be quite different depending on the algorithm used for calculation. Applicants have referred to various % identities, but there is no indication of the utilized algorithm to calculate the identity sequences. Furthermore, the calculation of "identity" is affected by variables such as the relative weight given to the sequence gaps versus mismatches, or whether conservative substitutions are weighted differently from non-conservative substitutions.

26. In the instant case, Specification does not teach or give an adequate guidance regarding how 80% homology or 95% homology has been calculated for SEQ ID NO: 1 & 2.

27. 5) Scope of the claims.

28. The claims broadly read on any or all nucleotide having a 80% homology to SEQ ID NO: 1 or 2, or pair of primer comprising a pair of nucleotide sequence, wherein the pair of nucleotide sequences have 95% homology to SEQ ID NO: 1 and 2 or have a one base of SEQ ID Nos: 1 and 2.

29. 6) & 7) Nature of the invention and level of skill in the art.

Art Unit: 1648

30. The invention involves a specific detection of EBV by using the molecular biology at least master degree. While the technique for nucleic acid hybridization or PCR is known in the art, it requires the precise structure of probe or primer being known for performer to calculate and select a suitable hybridization or PCR conditions to get a specific results.

31. Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled. it would required a person skill in the art to do undue experimentation to practice the full scope of the invention. it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

### ***Claim Rejections - 35 USC § 102***

32. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

33. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Sorge et al. (WO 95/16028A1).

34. Sorge et al. disclose a pair of oligonucleotide sequences SEQ ID NO: 28 and 29, in which SEQ ID NO: 29 having 100% homology to the SEQ ID NO: 2. Since the sequences of SEQ ID NO: 29 has an identical structure to the claimed oligonuceotide of SEQ ID NO: 2, it inherently has same biological characteristic for being able to hybridize with the nucleotide sequence of EBV (see Table 16 on page 35). Therefore, the claimed invention is anticipated by the cited reference.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.



Application/Control Number: 10/074,620

Page 8

Art Unit: 1648

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

  
Art Unit 1648

August 21, 2003